

IN THE CLAIMS

This listing of the claims replaces all prior versions of the claims in the application.

1. (currently amended): An immunogenic fusion protein comprising (a) a modified NS3 polypeptide comprising at least one amino acid substitution to the HCV NS3 region, such that protease activity is inhibited, and (b) at least one polypeptide derived from a region of the HCV polyprotein other than the NS3 region, wherein the fusion protein comprises sequences that are not in the order in which they occur naturally in the HCV polyprotein.

2. (original): The fusion protein of claim 1, wherein the modification comprises a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full-length HCV-1 polyprotein.

3. (currently amended): The fusion protein of claim 1, wherein the protein comprises a modified NS3 polypeptide, an NS4 polypeptide, an NS5a polypeptide, and optionally a core polypeptide.

4. (currently amended): The fusion protein of claim 3, wherein the protein further comprises an NS5b polypeptide, and optionally a core polypeptide.

5-10. (canceled)

11. (currently amended): The fusion protein of claim 1, wherein the polypeptides of (a) and (b) are derived from the same HCV isolate.

12. (currently amended): The fusion protein of claim 1, wherein at least one of the polypeptides present in the fusion is derived from a different isolate than the modified NS3 polypeptide.

13. (currently amended): An immunogenic fusion protein consisting essentially of, in amino terminal to carboxy terminal direction:

- (a) a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full-length HCV-1 polyprotein such that protease activity is inhibited, an NS4 polypeptide, and an NS5a polypeptide, wherein at least one of the polypeptides present in the fusion is from a different isolate than the modified NS3 polypeptide; or
- (b) a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full-length HCV-1 polyprotein such that protease activity is inhibited, an NS4 polypeptide, an NS5a polypeptide and an NS5b polypeptide, wherein at least one of the polypeptides present in the fusion is from a different isolate than the modified NS3 polypeptide;
- (c) an E2 polypeptide, a p7 polypeptide, an NS2 polypeptide, a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full-length HCV-1 polyprotein such that protease activity is inhibited, an NS4 polypeptide, and an NS5a polypeptide;
- (d) an E1 polypeptide, an E2 polypeptide, a p7 polypeptide, an NS2 polypeptide, a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full-length HCV-1 polyprotein such that protease activity is inhibited, an NS4 polypeptide, and an NS5a polypeptide;
- (e) an E2 polypeptide, a p7 polypeptide, an NS2 polypeptide, a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full-length HCV-1 polyprotein such that protease activity is inhibited, an NS4 polypeptide, an NS5a polypeptide and an NS5b polypeptide;
- (f) an E1 polypeptide, an E2 polypeptide, a p7 polypeptide, an NS2 polypeptide, a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full-length HCV-1

~~polyprotein such that protease activity is inhibited, an NS4 polypeptide, an NS5a polypeptide and an NS5b polypeptide;~~

~~(g) an E2 polypeptide and a modified NS3 polypeptide comprising substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full length HCV-1 polyprotein such that protease activity is inhibited;~~

~~(h) an E1 polypeptide, an E2 polypeptide and a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full length HCV-1 polyprotein such that protease activity is inhibited;~~

~~(i) an E2 polypeptide, a p7 polypeptide, an NS2 polypeptide and a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full length HCV-1 polyprotein such that protease activity is inhibited; or~~

~~(j) an E1 polypeptide, an E2 polypeptide, a p7 polypeptide, an NS2 polypeptide and a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full length HCV-1 polyprotein such that protease activity is inhibited.~~

14. (currently amended): An immunogenic fusion protein consisting essentially of, in amino terminal to carboxy terminal direction:

(a) a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full-length HCV-1 polyprotein such that protease activity is inhibited, an NS4 polypeptide, an NS5a polypeptide, and a core polypeptide; or

(b) a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full-length HCV-1 polyprotein such that protease activity is inhibited, an NS4 polypeptide, an NS5a polypeptide, an NS5b polypeptide and a core polypeptide;

~~(c) an E2 polypeptide, a p7 polypeptide, an NS2 polypeptide, a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-~~

~~1105 and/or Ser 1165, numbered relative to the full length HCV-1 polyprotein such that protease activity is inhibited, an NS4 polypeptide, an NS5a polypeptide and a core polypeptide;~~

~~(d) an E1 polypeptide, an E2 polypeptide, a p7 polypeptide, an NS2 polypeptide, a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full length HCV-1 polyprotein such that protease activity is inhibited, an NS4 polypeptide, an NS5a polypeptide and a core polypeptide;~~

~~(e) an E2 polypeptide, a p7 polypeptide, an NS2 polypeptide, a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full length HCV-1 polyprotein such that protease activity is inhibited, an NS4 polypeptide, an NS5a polypeptide, an NS5b polypeptide and a core polypeptide;~~

~~(f) an E1 polypeptide, an E2 polypeptide, a p7 polypeptide, an NS2 polypeptide, a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full length HCV-1 polyprotein such that protease activity is inhibited, an NS4 polypeptide, an NS5a polypeptide, an NS5b polypeptide and a core polypeptide;~~

~~(g) an E2 polypeptide, a modified NS3 polypeptide comprising substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full length HCV-1 polyprotein such that protease activity is inhibited, and a core polypeptide;~~

~~(h) an E1 polypeptide, an E2 polypeptide, a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full length HCV-1 polyprotein such that protease activity is inhibited, and a core polypeptide;~~

~~(i) an E2 polypeptide, a p7 polypeptide, an NS2 polypeptide, a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His-1083, Asp-1105 and/or Ser-1165, numbered relative to the full length HCV-1 polyprotein such that protease activity is inhibited, and a core polypeptide; or~~

(+) ~~an E1 polypeptide, an E2 polypeptide, a p7 polypeptide, an NS2 polypeptide, a modified NS3 polypeptide comprising a substitution of an amino acid corresponding to His 1083, Asp 1105 and/or Ser 1165, numbered relative to the full length HCV-1 polyprotein such that protease activity is inhibited, and a core polypeptide.~~

15. (canceled)

16. (original): A composition comprising an immunogenic fusion protein according to claim 1 in combination with a pharmaceutically acceptable excipient.

17. (original): A composition comprising an immunogenic fusion protein according to claim 13 in combination with a pharmaceutically acceptable excipient.

18. (original): A composition comprising an immunogenic fusion protein according to claim 14 in combination with a pharmaceutically acceptable excipient.

19. (withdrawn): A method of stimulating a cellular immune response in a vertebrate subject comprising administering a therapeutically effective amount of the composition of claim 16.

20. (withdrawn): A method of stimulating a cellular immune response in a vertebrate subject comprising administering a therapeutically effective amount of the composition of claim 17.

21. (withdrawn): A method of stimulating a cellular immune response in a vertebrate subject comprising administering a therapeutically effective amount of the composition of claim 18.

22. (original): A method for producing a composition comprising combining the immunogenic fusion protein of claim 1 with a pharmaceutically acceptable excipient.

23. (original): A method for producing a composition comprising combining the immunogenic fusion protein of claim 13 with a pharmaceutically acceptable excipient.

24. (original): A method for producing a composition comprising combining the immunogenic fusion protein of claim 14 with a pharmaceutically acceptable excipient.

25-40. (canceled)

41. (currently amended): An immunogenic fusion protein comprising (a) a modified NS3 domain comprising a substitution of an amino acid corresponding to Ser-1165, numbered relative to the full-length HCV-1 polyprotein, such that protease activity is inhibited; (b) an NS4 domain; (c) an NS5a domain; (d) an NS5b domain; and (e) optionally a core polypeptide comprising the sequence of amino acids depicted at amino acid positions 1772-1892 of SEQ ID NO:6.

42. (previously presented): The immunogenic fusion protein of claim 41, wherein said protein comprises a core polypeptide consisting of the sequence of amino acids depicted at amino acid positions 1772-1892 of SEQ ID NO:6.

43-44. (canceled)

45. (previously presented): A composition comprising an immunogenic fusion protein according to claim 41 in combination with a pharmaceutically acceptable excipient.

46. (canceled)

47. (withdrawn): A method of stimulating a cellular immune response in a vertebrate subject comprising administering a therapeutically effective amount of the composition of claim 45.

48. (canceled)

49. (previously presented): A method for producing a composition comprising combining the immunogenic fusion protein of claim 41 with a pharmaceutically acceptable excipient.

50-58. (canceled)

59. (new): An immunogenic fusion protein comprising (a) a modified NS3 polypeptide comprising at least one amino acid substitution to the HCV NS3 region, such that protease activity is inhibited, and (b) at least one polypeptide from a region of the HCV polyprotein other than the NS3 region, wherein at least one polypeptide is from the core region of the HCV polyprotein, and the fusion protein comprises sequences not in the order in which they occur naturally in the HCV polyprotein.